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EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/080,797	BRAZZELL ET AL.	
	Examiner	Art Unit	
	J. Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,7,8,27-33,38-41 and 43-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,7,8,27-33,38-41 and 43-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This Action is in response to the communication filed on 12/17/03. The amendment has been entered. Claims 4-6, 9-26, 34-37 and 42 have been cancelled. New claims 43-50 have been added. Claims 1-3, 7, 8, 27-33, 38-41 and 43-50 are currently pending in the application and are examined herein.

2. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-3, 7, 8, 27, 28, 30 and 31 remain rejected and new claims 43-47 are now rejected under 35 U.S.C. 102(b) as being anticipated by Leboulch et al. (WO 99/26480, cited as IDS reference AN).

1. As indicated in the previous Office Action, Leboulch teaches a method for treating a human patient suffering from diabetic retinopathy (which can result in corneal, retinal and iris neovascularization) by administering a to said patient a nucleic acid molecule which expresses endostatin wherein expression of the endostatin polypeptide in the patient inhibits angiogenesis in the vicinity of the retina (e.g., see claim 33, page 33-34). Specifically, Leboulch teaches that

the gene therapy vector can be a retroviral vector, adenoviral vector or adenoviral-associated vector (AAV) (see p. 5, lines 19-21). Furthermore, Leboulch indicates that the gene therapy vector can be administered by any method that allows the vector to reach the target cells, such as injection to the target tissue, wherein the target tissue can be the retina of the eye (e.g., see p. 11, lines 10-22; and p. 14, lines 2-14; and claim 33). Therefore, Leboulch anticipates the instant claims.

Response to Arguments

2. Applicant's arguments filed 12/17/03 have been fully considered but they are not persuasive. Applicants' argue that the reference does not provide an enabling disclosure for the direct administration of a viral vector to the eye to treat ocular neovascularization. Additionally, Applicants' argue since the reference allegedly is not enabled, the reference does not place the place the claimed invention in the hands of the public, and thus, the reference does not anticipate the claimed invention.

3. In response, it is respectfully pointed out that although Applicants contend that the reference is not enabled, MPEP 2121 indicates,

> "When the reference relied on expressly anticipates or makes obvious all of the elements of the claimed invention, the reference is presumed to be operable. Once such a reference is found, the burden is on applicant to provide facts rebutting the presumption of operability. In re Sasse, 629 F.2d 675, 207 USPQ 107 (CCPA 1980). See also MPEP § 716.07."

In the instant case, Applicants have only asserted that the reference is not enabled and have not provided facts to rebut the presumption of operability. Therefore, the rejection is not withdrawn.

New Grounds of Rejections

Claim Rejections - 35 USC § 112, second paragraph

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1, 7, 33, 38-41 and 48-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, claims 39-41 recite the limitation "said bovine immunodeficiency viral vector", claims 48-50 recite the limitation "the lentiviral vector" There is insufficient antecedent basis for these specific limitations in the claims. Claims 39-41 and 48-50 depend on claims 1, 7, and 33, therefore, claims 1, 7 and 33 are also rejected for encompassing all of the limitations of claim 39-41 and 48-50, including the limitations for which there is no antecedent basis.

It is noted that changing the claims such that instead of claiming vectors "obtained from" the viruses, specifically claiming that the vectors are the specific viral vectors (e.g., the viral vector is an adenoviral vector rather than is obtained from an adenovirus) would obviate the rejections under 35 USC 112, second paragraph.

Claim Rejections - 35 USC § 112, first paragraph

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 7, 8, 33, 38-41, 43-44 and 48-50 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

8. Claim 7 has been amended to indicate that the viral vector is "obtained from a virus", claim 8 further indicates the vector is "obtained from an adenovirus", claim 33 further indicates the vector is "obtained from a lentivirus", claim 38 further indicates the vector is "obtained from a bovine immunodeficiency virus", claim 43 further indicates the vector is "obtained from a adeno-associated virus", claim 44 further indicates the vector is "obtained from a retrovirus". The instant claims encompass methods using viral vectors wherein the viral vectors are "obtained from" specific viruses. However, the specification does not explicitly or implicitly describe any vectors which can be "obtained from" a virus. Additionally, the specification does not particularly define the phrase "obtained from" with respect to the claimed viral vectors, thus there is no implicit description of the term "obtained from" with respect to the described vectors. Therefore, the specification does not have proper support for any vectors "obtained from" the viruses as set forth in the instant claims and, as such, the claims are rejected under 35 USC 112, first paragraph (new matter). For instance, one of ordinary skill in the art would not know what a vector "obtained from a virus" (such as one obtained from an adenovirus, lentivirus, BIV or AAV) would encompass without a proper description in the specification. As written, the claim could encompass a viral vector such as an adenoviral vector, but the claims could also

encompass vectors that were merely "obtained" from the viral vectors, such as viral elements, including the capsid, or other genes expressed by the virus.

Claims 39-41 and 48 –50 are dependent claims. It is noted that claim 7 depends on claim 1, therefore, claim 1 must encompass the limitations of claim 7 and, as such, claim 1 is rejected for the same reasons.

Claim Rejections - 35 USC § 112, first paragraph

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-3, 7, 8, 27-33, 38-41 and 43-50 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

METHOD 1: A method for ameliorating ocular neovascularization (or choroidal neovascularization (CNV)) in an individual afflicted with ocular neovascularization (or CNV) wherein said method comprises directly administering to the eye or eyes of said individual a viral vector that operably encodes and expresses endostatin such that said administering results in the amelioration of said ocular neovascularization (or CNV); and,

Method 2) A method for reducing the rate of ocular neovascularization (or choroidal neovascularization (CNV)) in an individual afflicted with ocular neovascularization (or CNV) wherein said method comprising administering directly to the eye of said individual a viral vector that operably encodes and expresses endostatin, wherein said

administering results in reducing the rate of said ocular neovascularization (or said CNV),

does not reasonably provide enablement for the full scope of the method encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. Specifically, the instant claims encompass "treating" ocular vascularization (or CNV) in a subject having the disorder. Looking to the specification for guidance, it is clear the "treating" encompasses "amelioration" as well as "protection, in whole or in part against further ocular neovascularization" (including CNV) (see paragraph bridging pages 2-3 or the specification). Therefore, it is clear the "treating" encompasses preventing any future occurrence of ocular neovascularization (or CNV). However, the specification has not enabled one of skill in the art to prevent any future occurrence of ocular neovascularization (or CNV) for the reasons below.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988).

Wands states on page 1404,
"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The instant claims are drawn to a method of treating ocular neovascularization by administering a viral vector encoding endostatin. As indicated above, the specification defines "treating" as encompass protecting in whole or in part, any future occurrence of ocular neovascularization (or CNV). Therefore the general nature of the invention encompasses preventing any future occurrence of ocular neovascularization (or CNV).

The breadth of the claims

The presently pending claims are very broad and encompass treating any type of ocular neovascularization by administering any type of viral vector encoding endostatin wherein said viral vector is administered to the eye of the subject having the neovascular disorder. Furthermore, the claims encompass prophylactic treatment (i.e. preventing) as well as therapeutic amelioration of ocular neovascularization.

The unpredictability of the art and the state of the prior art

The relevant prior art indicates that methods of gene therapy for the eye at the time of invention were highly unpredictable. For instance, Ashton (1998, cited in IDS as reference AR) teaches,

> "The eye barriers greatly limit ocular exposure to topically and systemically applied compounds. This necessitates the administration of high does to achieve therapeutic ocular levels and the resulting high systemic exposure can then reduce the therapeutic index of otherwise promising agents." (see lines 1-5 of Abstract)

Additionally, Wright (Brit. Journ. Opthalmol. 1997, Vol. 81, No. 8, pages 620-623.) indicates a number of problems related to gene therapy for the eye. For instance, Wright teaches,

> "As long term gene expression is the goal, success depends on (i) efficient uptake into the target cells, (ii) avoidance of endocytosis and lysosomal degradation, (iii) import into the

> nucleus, (iv) stable retention in the nucleus, either as a circular episome (for example adenovirus) or by integration into the host genome, (v) target cell specific expression the therapeutic gene, driven by the natural promoter and enhancer elements, (vi) appropriate translation and subcellular localization of the gene product. The most difficult steps are probably (iii), (iv) and (v)." (See p. 620, first column).

Regarding the long term expression of a reporter gene in the eye using an adenoviral vector, Wright teaches, "Transgene expression declined with time because of factors such as low grade immune reaction, switch off, or loss of the episomal transgene." (See p. 621, first column). Wright also indicates that the future of gene therapy for the eye will require additional work that is not a matter of routine experimentation. Specifically, Wright teaches,

> "It is difficult to predict the key ingredients required for success in retinal gene therapy. Less immunogenic vectors will certainly be helpful but one worrying possibility is that unless chromosomal integration of the introduced gene occurs, expression will be too short lived (fore example, not more than one year) to be useful. None of the currently used vectors (ABV, AAV, HSV1) integrates at an appreciable frequency , and although this can be seen as an advantage for dividing cells (less chance of oncogenic damage) it is probably a disadvantage in post-mitotic cell." (See p. 621 under "Future Developments")

As mentioned above, the claims also encompass prophylactic treatment (i.e. methods of preventing ocular neovascularization). Prophylactic methods encompass the prevention of any future occurrence of neovascularization. There are no examples presented in the instant specification or in the relevant prior art that gene therapy can be used to prevent all future occurrence of any disease for the entire life of an individual. Considering that such treatment would require the expression of a "preventative" amount of the therapeutic protein for the life of the individual and considering the teaching in the prior art that long term expression of a therapeutic molecule in eye cells is still a very challenging feat, it is highly unlikely that it would be a matter of routine experimentation to make a gene therapy construct that could be used to prevent any future occurrence of ocular neovascularization for the entire life of an individual.

Working Examples and Guidance in the Specification

The specification has working examples which disclosing: methods for reducing the amount of ocular neovascularization (or CNV) (i.e., ameliorating ocular neovascularization) in an individual afflicted with the disorder, and methods of reducing the rate of ocular neovascularization (or CNV) in an individual with the disorder (e.g., See Example 2, p. 19-22 and Example 8, p. 27).

Quantity of Experimentation

Considering the breadth of the claims and the unpredictable nature of gene therapy for the eye, and the limited amount of working examples and guidance provided, it is clear that additional experimentation would be required in order to practice the claimed method to the full scope encompassed by the claims. Specifically, additional experimentation would have to be performed in order to perfect methods of gene therapy preventing any future occurrence of ocular neovascularization (or CNV). Considering the teachings of the prior art (indicated above) it is highly unlikely that the additional experimentation is a matter of routine experimentation.

Level of the skill in the art

The level of the skill in the art is deemed to be high.

Conclusion

Considering the breadth of the claims, the high degree of unpredictability recognized in the art, the limited working examples and guidance provided (in view of the breadth of the claims); and the high degree of skill required, it is concluded that the amount of experimentation required to perform the broadly claimed invention is undue.

It is noted that amending the claims to be limited to the method(s) described above would obviate this rejection.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. Claims 1-3, 7, 27-29 and 44-47 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 6,201,104 (MacDonald et al.)

MacDonald teaches a method for treating ocular neovascularization (including choroidal neovascularization) in an eye of an individual by administering a retroviral vector that encodes and expresses endostatin, wherein the neovascularization can be corneal, retinal or iris neovascularization, and wherein the neovascularization can be cause by macular degeneration (among other things). (For example, see Column 2, lines 9-50; column 5, lines 9-67; column 11, lines 39-67; column 12, lines 41-65).

Therefore, MacDonald anticipates the instant claims.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 1, 7, 8, 30-32 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6,201,104 (MacDonald et al.) in view of US Patent 6,106,826 (Brandt et al.).

As mentioned above, MacDonald teaches a method for treating ocular neovascularization (including choroidal neovascularization) in an eye of an individual by administering a retroviral vector that encodes and expresses endostatin, wherein the neovascularization can be corneal, retinal or iris neovascularization, and wherein the neovascularization can be cause by macular degeneration (among other things). (For example, see Column 2, lines 9-50; column 5, lines 9-67; column 11, lines 39-67; column 12, lines 41-65).

MacDonald does not teach that the vector that is used to express endostatin is an adenoviral vector or adeno-associated viral vector. Nor does MacDonald specifically teach to administer the gene therapy vector intraocularly, subretinally or intravitreally.

Brandt teaches gene therapy vectors which can be used to deliver therapeutic genes for gene therapy, and specifically teaches an HSV vector as well as an adenoviral vector and adeno-associated vector for use in gene therapy of the eye wherein the vector can be delivered to the eye by intravitreally injecting the vector (which would necessarily encompass sub-retinal as well as intraocular delivery); as well as subretinally and intraocullarly delivering the vector, for therapeutic purposes, such as macular degeneration. (e.g., see abstract, column 5, lines 5-20, column 8,lines 57-65, and column 9 lines 15-20).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time of filing to modify the method taught by MacDonald such that the vector used was an adenoviral vector or AAV vector and such that the vector was delivered by intraocularly, subretinally, and/or intravitreally.

The motivation to modify the method of MacDonald is supplied in part by MacDonald who teaches general gene therapy methods for treating ocular neovascularization and in part by Brandt who specifically teaches that adenoviral and AAV vectors can be used to treat eye disease by intravitreally, subretinally or intraocullarly delivering the therapeutic vector.

16. Claims 1, 7, 33 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6,201,104 (MacDonald et al.) in view of US Patent 6,555,107 (Poeschla et al.).

As mentioned above, MacDonald teaches a method for treating ocular neovascularization (including choroidal neovascularization) in an eye of an individual by administering a retroviral vector that encodes and expresses endostatin, wherein the neovascularization can be corneal, retinal or iris neovascularization, and wherein the neovascularization can be cause by macular degeneration (among other things). (For example, see Column 2, lines 9-50; column 5, lines 9-67; column 11, lines 39-67; column 12, lines 41-65).

MacDonald does not teach that the vector that is used to express the therapeutic gene is a lentiviral vector, or that the vector is a bovine immunodeficiency viral vector.

Poeschla teaches methods of gene therapy for the eye wherein a lentiviral vector, specifically, a bovine immunodeficiency vector, is used to deliver and express the therapeutic gene in the eye of the subject. (For example, see abstract, column 2, lines 10-35; column 4, lines 34-41; column 11, 45-55).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time of filing to modify the teaching of MacDonald such that the bovine immunodeficiency viral vector taught by Poeschla (which is a lentiviral vector) is used to deliver and express the therapeutic gene.

The motivation to make such a modification is provided by Poeschla. Poeschla teaches that the BIV vector is better for transfecting difficult to target non-dividing cells of the nervous system including eye cells.

17. Claims 1, 7, 33 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6,201,104 (MacDonald et al.) in view of US Patent 6,555,107 (Poeschla et al.) and US Patent 6,106,826 (Brandt et al.).

As mentioned above, MacDonald teaches a method for treating ocular neovascularization (including choroidal neovascularization) in an eye of an individual by administering a retroviral vector that encodes and expresses endostatin, wherein the neovascularization can be corneal, retinal or iris neovascularization, and wherein the neovascularization can be cause by macular degeneration (among other things). (For example, see Column 2, lines 9-50; column 5, lines 9-67; column 11, lines 39-67; column 12, lines 41-65).

MacDonald does not teach that the vector that is used to express the therapeutic gene is a lentiviral vector, or that the vector is a bovine immunodeficiency viral vector. Nor does MacDonald teach to deliver the vector by injecting the vector intravitreally, intraocullarly, or subretinally.

Poeschla teaches methods of gene therapy for the eye wherein a lentiviral vector, specifically, a bovine immunodeficiency vector, is used to deliver and express the therapeutic gene in the eye of the subject. (For example, see abstract, column 2, lines 10-35; column 4, lines 34-41; column 11, 45-55).

Brandt teaches gene therapy vectors which can be used to deliver therapeutic genes for gene therapy, and specifically teaches an HSV vector as well as an adenoviral vector and adeno-associated vector for use in gene therapy of the eye wherein the vector can be delivered to the eye by intravitreally injecting the vector (which would necessarily encompass sub-retinal as well as intraocular delivery); as well as subretinally and intraocullarly delivering the vector, for

therapeutic purposes, such as macular degeneration. (e.g., see abstract, column 5, lines 5-20, column 8,lines 57-65, and column 9 lines 15-20).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time of filing to modify the teaching of MacDonald such that the bovine immunodeficiency viral vector taught by Poeschla (which is a lentiviral vector) is used to deliver and express the therapeutic gene and to deliver the lentiviral/BIV vector by intravitreally, subretinally or intraocullarly injecting the gene therapy vector.

The motivation to make such a modification is provided in part by MacDonald who teaches general gene therapy methods for treating ocular neovascularization; in part by Brandt who specifically teaches that adenoviral and AAV vectors can be used to treat eye disease by intravitreally, subretinally or intraocullarly delivering the therapeutic vector; and in part by Poeschla who teaches that the BIV vector is better for transfecting difficult to target non-dividing cells of the nervous system including eye cells.

Miscellaneous

The objection to the claims is withdrawn in view of the amendment.

The rejection of claims under 35 USC second paragraph (as previously set forth) are withdrawn in view of the claim amendments. However, new grounds of rejection under 35 USC 112, second paragraph are set forth herein.

The rejection of claims under 35 USC 112, first paragraph with respect to the written description of functionally active endostatin fragments/variants (as well as the related

enablement rejection) is withdrawn in view of the amendment indicating functionally active endostatin and in view of the state of the art of functionally active endostatin variants.

The rejection of claims under 35 USC 112, first paragraph for lack of enablement has been modified as set forth herein. Applicants indicated that they amended the claims to overcome the rejection, however, upon further consideration, the specification clearly indicates that "therapeutic treatment" encompasses preventing any future occurrence of ocular neovascularization. Therefore, the rejection has been modified as indicated herein. It is pointed out that amending the claims such that the claims do not read on preventing any future occurrence of ocular neovascularization (such as indicated herein) would obviate the rejection.

The rejection of claims under 35 USC 102(b) are not withdrawn for the reasons indicated herein.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (571) 272-0756. The examiner can normally be reached on M-F (8:00-5:30) with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (571) 272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon Eric Angell, Ph.D.
ART UNIT 1635